TMA DoD Pharmacoeconomic Center
Fort Sam Houston, TX

MTF Quarterly Webcast
June 16, 2011

LTC Stacia Spridgen
Director, DoD Pharmacoeconomic Center

Introduction

- Greetings from the PEC
- Purpose of the Quarterly MTF Webcast
- DCO Ground Rules
  - Type questions into the DCO system
  - Put on mute, not on hold
  - Contingency plan if DCO system quits working

Topic Outline

- Introduction from Director, PEC (LTC Spridgen)
- MTF Corner – Electronic Prescribing (eRx) & MTF-MOP Update (Mr. Gibbs)
- Review of February 2011 P&T Meeting (Dr Meade)
- Overview of May 2011 P&T Meeting (Dr Meade)
- Closing the Loop on Formulary Decisions (Dr Trice)
- Miscellaneous items
  - Update on PEC Uniform Formulary webpage (Dr Briggs)
  - Update on Pradaxa (Dr Allerman)
  - Future Webcast: MTF Prescription Restriction Program (Dr Hearin)

MTF Corner

Electronic Prescribing (eRx) & MTF-MOP Update

Henry Gibbs
Director, DoD Pharmacy Informatics

eRx: DoD Definition

- Allow electronic prescribing from all points of order entry - civilian and Military Treatment Facility (MTF) - to all points of dispensing (MTF, mail order, and retail)

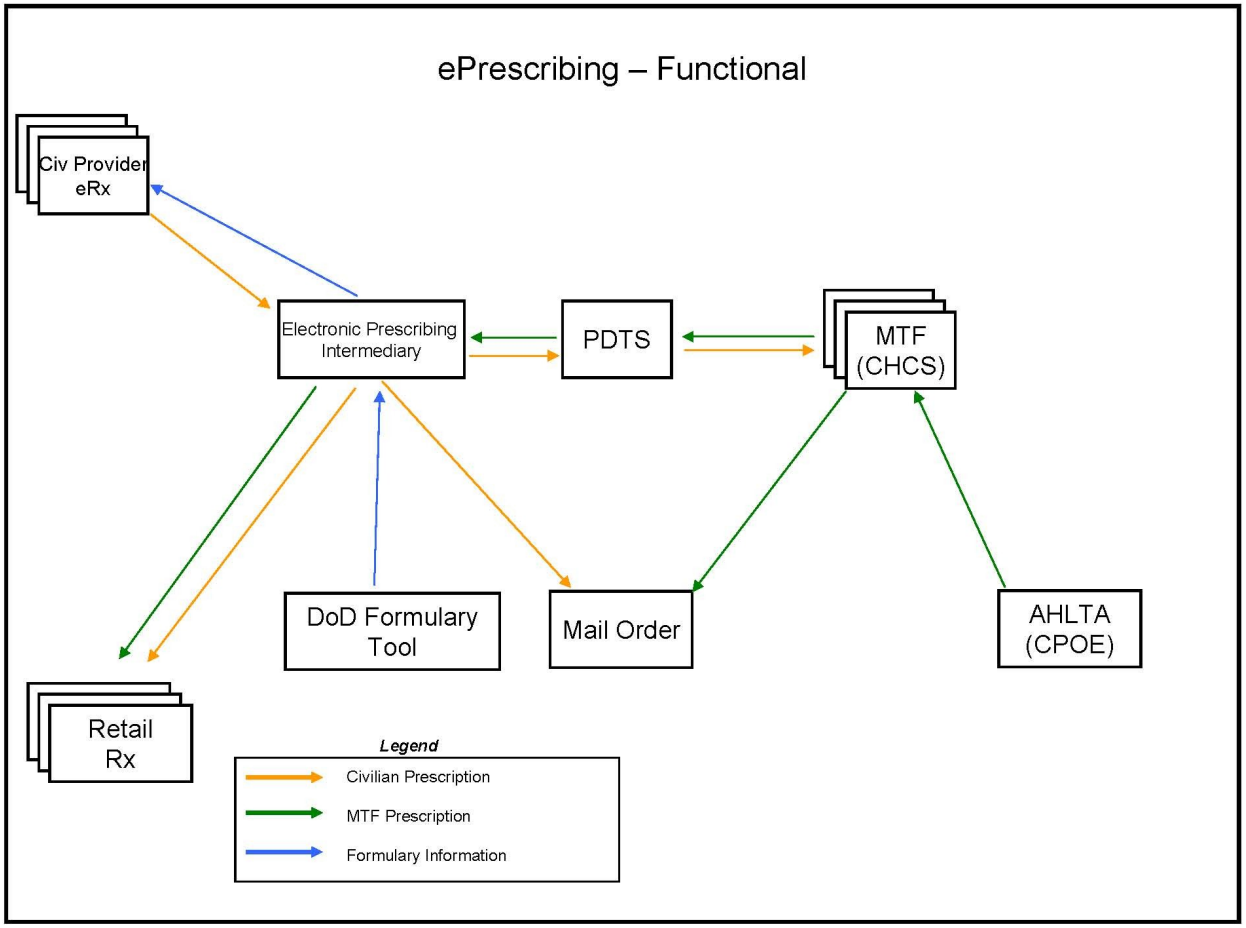
eRx: Trends

- Adoption of electronic prescribing by civilian providers (according to Surescripts ®)
  - 16,000 providers in 2006
  - 36,000 providers in 2007
  - 74,000 providers in 2008
  - 140,000 providers in 2009
  - 200,000 providers in 2010 (as of September 2010)
- The Medicare Improvements for Patients and Providers Act of 2008 (MIPPA)
  - Incentives for providers to e-prescribe in 2009 through 2013 (higher reimbursement rates)
  - Imposes penalties beginning in 2012 for providers that are not utilizing electronic prescribing
- Currently MTFs cannot receive electronic prescriptions from civilian providers

eRx: Goals

- Leverage existing MHS infrastructure
  - Modernize the PDTS to support routing of electronic prescriptions from civilian providers to Military Treatment Facility (MTF) pharmacies and from MTF providers to retail pharmacies
  - PDTS will be the DoD eRx intermediary
- Develop a solution that will support electronic prescribing today (CHCS) and future (EHR way ahead)

eRx– Functional View



eRx: Status

- Decision Paper has been drafted
  - Seeking Leadership approval
- Need to identify funding for eRx initiative
- Coordinate contracting efforts between program offices
  - Similar to MTF-TMOP project

MTF–MOP Transfer

- MTF to Mail Order Pharmacy (MOP) Transfer Initiative
  - Allow for the electronic transfer of MTF refill prescriptions to TRICARE Mail Order Pharmacy
    - First fill must occur at MTF; all subsequent fills can be transferred to TMOP
    - Transfer request is initiated by beneficiaries via AudioCARE™ System or pharmacy personnel in CHCS
    - Upon successful transfer all TMOP business rules apply (i.e. applicable co-pays)
  - Implementation
    - CHCS Test Site → Camp LeJeune
    - CHCS Software available to all MTFs (December 2010)
    - MTFs interested need to coordinate with TMA, Pharmaceutical Operations Directorate
      - "Implementation Guide" → provide pharmacy understanding of LOE (setup/ maintenance)

Contact Information

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Review of February 2011 P&T Activities

Dave Meade, PharmD, BCPS
Clinical Pharmacist

February 2011
DoD P&T Committee Meeting

- **Uniform Formulary Class Reviews**
  - Gastrointestinal-1 Agents (GI-1s)
  - Pancreatic Enzyme Products (PEPs)
  - Antilipidemic-2 Agents (LIP-2s)
    - Fibric Acid Derivatives
    - Rx Omega-3 fatty acids
    - Bile acid sequestrants

February 2011
DoD P&T Committee Meeting

- **New Drugs in Previously Reviewed Classes**
  - Aliskiren/amlodipine (Tekamlo)
  - Amlodipine/olmesartan/hydrochlorothiazide (Tribenzor)
  - Self-monitoring Blood Glucose System Test Strips and Meters
  - Donepezil (Aricept 23 mg)
  - Ondansetron Oral Soluble Film (Zuplenz)

Uniform Formulary Class Reviews: Gastrointestinal-1 Drugs (GI-1)

Class Definition

Drug Class	Generic Name	Brand Name	Generic
Aminosalicylates	Sulfasalazine	Azulfidine Azulfidine EN	Yes
	Balsalazide	Colazal	Yes
	Olsalazine	Dipentum	Patent Expired
	Oral Mesalamine Rectal Mesalamine	Asacol, Asacol HD Apriso Lialda Pentasa Canasa Rowasa sfRowasa	No No No Patent Expired Patent Expired Yes No
GI-Steroids	Budesonide	Entocort EC	No
	Hydrocortisone	Cortenema Cortifoam	Yes
Miscellaneous agents	Alosetron	Lotronex	No
	Tegaserod	Zelnorm	Withdrawn from market

Overall Clinical Effectiveness Conclusion

- **5-ASAs**
  - Aminosalicylates are effective in induction and maintenance of remission in active ulcerative colitis. No differences in efficacy b/w sulfasalazine and newer 5-ASAs, but 5-ASAs are better tolerated
  - Differences in drug delivery technology do not confer additional benefit in terms of clinical response
  - 5-ASA formulations are not effective for inducing remission in active Crohn's disease
  - No clinically relevant differences b/w the newer 5-ASAs in terms of safety
  - Treatment choice depends on location and severity of disease & patient preference

- **Topical Steroids**
  - Oral budesonide (Entocort EC) has fewer systemic effects than the other oral corticosteroids (e.g., prednisone) and is delivered directly to the colon. It is effective and safe for Crohn's disease. Tx is limited to 3 months
  - The rectally administered hydrocortisone enema and foam preparations which are effective and safe for the treatment of distal ulcerative colitis

- Alosetron (Lotrenex) and Tegaserod (Zelnorm) have severe AEs; alosetron is available under a REMs program. Tegaserod with a treatment IND from FDA

Gastrointestinal-1 -Drugs Final Decision

DoD PEC Drug Class	BCF	UF	NF	PA and QL Issues	Comments
GI-1s	Aminosalicylates ▪Mesalamine (Asacol)	Aminosalicylates ▪Sulfasalazine/EC (Azulfidine, Azulfidine EN generic) ▪Balsalazide (Colazal, generic) ▪Olsalazine (Dipentum) ▪Mesalamine (Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, Rowasa, sfRowasa enema) GI-Steroids ▪Budesonide (Entocort EC) ▪Hydrocortisone enema and foam (Cortenema, generic; Cortifoam, generic) Miscellaneous Agents ▪Alosetron (Lotronex)	None	None	Asacol is BCF; all others remain UF Note: Tegaserod (Zelnorm) no longer commercially available; available under treatment INF application to the FDA. If approved by FDA, sent directly to the patient by the manufacturer

Uniform Formulary Class Reviews: Pancreatic Enzyme Products (PEPs)

Class Definition

Characteristic	Creon (Brand)	Pancreaze (Brand)	Zenpep (Brand)
Manufacturer	Abbott	McNeil Pediatrics	Eurand
FDA -approved Indications	• EPI due to CF, or other conditions • Chronic pancreatitis • Pancreatectomy	• EPI due to CF, or other conditions	• EPI due to CF, or other conditions
FDA Approval Date	April 30, 2009	April 12, 2010	Aug 27, 2009
Patent Expiration	Not listed	Not listed	February 20, 2028
Generics	No	No	Yes (authorized generic) Pancrelipase 5,000 lipase units; distributed by X-Gen

EPI: exocrine pancreatic insufficiency
CF: cystic fibrosis

Overall Clinical Effectiveness Conclusion

- Based on clinical efficacy alone, Creon, Pancreaze, and Zenpep are effective at increasing CFA in patients with EPI, compared to placebo. There are no head-to-head trials
- With regards to safety, the available evidence suggests there are no clinically relevant differences between Creon, Pancreaze, and Zenpep
- With regards to other factors such as microsphere size, and storage requirements/stability, there are no clinically relevant differences between the PEPs
- Zenpep has information for G-tube administration, but is currently under FDA review
- Pancreaze is the only PEP which has efficacy and safety data in children as young as 6 months
- MHS utilization is primarily in the population older than 45 years

CFA: Coefficient of fat absorption

Pancreatic Enzyme Products Final Decision

DoD PEC Drug Class	ECF	UF	NF	PA and QL Issues	Comments
Pancreatic Enzyme Products	Pancreaze	▪ Creon ▪ Zenpep	None	None	Pancreaze is ECF; all others are UF

Uniform Formulary Class Reviews: Antilipidemics-2 (LIP-2s)

Class Definition

Generic name	Brand name	Generic	Patent exp
Fibric Acid Derivatives			
Gemfibrozil	Lopid	Yes	
Fenofibrate nonmicronized	Lofibra (branded generic)	Yes	
Fenofibrate micronized	Lofibra (branded generic)	Yes	
	Antara	No	2020
Fenofibrate IDD-P	Triglide	No	2021
Fenofibrate nanocrystallized	Tricor	No	Jan 25, 2011-Feb 21, 2023
Fenofibrate meltdose	Fenoglide	No	2024
Fenofibrate Lidose	Lipofen	No	2015
Fenofibric acid	Fibricor	No	2027
Fenofibric acid (choline salt)	Trilipix	No	2025
Omega-3 Fatty Acids			
Omega-3 fatty acid	Lovaza (formerly Omacor)	No	2013 - 2025
Bile Acid Sequestrants			
Cholestyramine/sucrose	Questran	Yes	
Cholestyramine/aspartame	Questran Light, Prevalite	Yes	
Colestipol	Colestid	Yes	2013
Colesevelam	Welchol	No	2014 -2022

MTF Issues
Lovaza vs. Supplements

- Can fish oil be substituted for Lovaza?
  - OTC fish-oil supplements containing equivalent amounts of EPA/DHA to Lovaza should be therapeutically interchangeable, but concerns about issues such as potency, capsule counts, batch-to-batch consistency, and purity/ truth in labeling remain
- Non prescription drugs are not a covered TRICARE benefit

USP– Verified Fish Oil Products

Fish Oil Product	Prime Vendor?	Where Available	PV Price/4GM
Berkley & Jensen	No	BJ's	N/A
Equaline/Nutriplus	No	Acme/Albertsons/ Jewel/Osco/Savon	N/A
Kirkland Signature Fish Oil Concentrate	No	Costco	N/A
Kirkland Signature Fish Oil Enteric Coat	No	Costco	N/A
Nature Made	Yes	Many Locations	$0.52
Nature Made Odorless	Yes	Many Locations	$0.94
Nature Made Double Strength	Yes	Many Locations	$0.47
Nature Made Super Strength Omega-3 EPA	Yes	Many Locations	$1.00
Major Cholesterol Free*	Yes	Many Locations	$0.34

*Not USP Verified; Primary product used at the

Lovaza
Overall Clinical Effectiveness Conclusion

- Efficacy
  - Lovaza decreases TG by 45%; increase LDL by up to 45%
  - Inconclusive evidence for CHD prevention
  - Definitive studies to determine the efficacy of Lovaza in different psychiatric disorders are needed
- Safety
  - GI problems most common AE
- The DoD P&T Committee concluded that the use of Lovaza for psychiatric uses, cardioprotective effects or uses other than for patients with TG >500 mg/dL is not supported by the available evidence

Prior Authorization Criteria Lovaza

- Lovaza allowed only for the FDA-approved indications. All current and new users of Lovaza must meet one of the following criteria to pass through the PA process.

- Patients with TG > 500 mg/mL who are receiving statins AND have had an inadequate TG-lowering response to a therapeutic trial of niacin (1-2 g/day) or fibrates, are unable to tolerate niacin or fibrates, or are not candidates for niacin or fibrate therapy.

- Patients with TG > 500 mg/mL who are not receiving statins AND who have had an inadequateTG-lowering response to a therapeutic trial of monotherapy with both a fibrate and niacin, are unable to tolerate niacin and fibrates, or are not candidates for niacin and fibrate therapy.

- Coverage is not approved for the use of Lovaza for the treatment of other conditions, including:

  ADHD, Alzheimer’s disease, Bipolar disorder, Crohn's disease, Cystic fibrosis, Dementia, Depression, Inflammatory bowel disease, Intermittent claudication, Metabolic syndrome, Osteoporosis, PTSD, Renal disease (IgA Nephropathy), Rheumatoid arthritis, Schizophrenia, Type 2 diabetes mellitus and Ulcerative colitis

Fibric Acid Derivatives

Overall Clinical Effectiveness Conclusion

- Efficacy
  - Fenofibrate formulations
    - The fenofibrate formulations are bioequivalent to one another
      - Similar pharmacokinetics, efficacy and safety profiles
      - Any fenofibrate would meet the needs of the majority of our patients in the DoD
  - Gemfibrozil vs. Fenofibrates
    - Both reduce TG by 20 -50%, raise HDL by 10 -20% and decrease LDL by 5-20%
    - Gemfibrozil has been shown to reduce nonfatal MI and CHD death. Fenofibrates reduce nonfatal MI and, in combination with a statin, may benefit individuals with TG > 204 mg/dl and HDL < 34 mg/dl
- Safety/Tolerability
  - Although data suggest that gemfibrozil is more likely to interact with statin than fenofibrates, there is lack of clinical evidence to support that the incidence of myopathy/rhabdomyolysis is lower with fenofibrate
- Other Factors
  - Major concern is the continuous fenofibrate supply disruptions
  - For patients requiring a fenofibrate, gemfibrozil and one fenofibrate formulation would be expected to meet the needs of our DoD patients

Prior Authorization Criteria Fibrates

- Preferred fibrates: gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra), & Tricor

- PA criteria apply to the nonpreferred fibric acid derivatives: Antara, Triglide, Lipofen, Fibricor, and Trilipix. Coverage would be approved if the patient met any of the following criteria:
  - Automated PA criteria:
    - The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or Tricor (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

  - Manual (paper) PA criteria, if automated criteria are not met:
    - The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

Bile Acid Sequestrants

Overall Clinical Effectiveness Conclusion

- Efficacy
  - Overall modest 15 to 30% LDL reduction by BAS monotherapy; replaced by statins
  - Colesevelam appears similar to older BAS, but no head to head comparison trials exist
  - Colesevelam is the only BAS approved to decrease A1C (0.5%) but other DM drug classes have greater efficacy
- Safety
  - Comparable GI distress caused by all (constipation, dyspepsia)
  - No current trials comparing the 3 BAS agents

Antilipidemics–2 drugs– Final Decision

BCF	UF	NF	PA and QL Issues	Comments
Fibric Acid Derivatives ▪ Gemfibrozil (Lopid, generics) ▪Fenofibrate nanocyrstallized (Tricor)	**Fibric Acid Derivatives** ▪Fenofibrate micronized/ nonmicronized (Lofibra, generics) ▪IDD-P (Triglide) ▪Micronized (Antara) ▪Lidose (Lipofen) ▪Fenofibric acid (Fibricor) ▪Choline fenofibric acid (Trilipix) **Omega-3 Fatty Acids** ▪Lovaza **Bile Acid Sequestrants** ▪Cholestyramine/ sucrose/aspartame (Questran, Questran Light, generics) ▪Colestipol (Colestid, generics)	**Bile Acid Sequestrants** ▪Colesevelam (Welchol) remain NF	Automated PA for Lovaza PA restricting Lovaza usage to the FDA-approved indication for all patients, new and existing users	Fibric Acids: Trial of generic fenofibrates, gemfibrozil, or Tricor mandated prior to use of a non step- preferred drugs: Triglide, Antara, Lipofen, Fibricor, and Trilipix

New Drugs In Previously Reviewed Classes

Aliskiren/Amlodipine Tablets (Tekamlo; Novartis)

Tekamlo

- Type of drug
  - Fixed-dose combination antihypertensive, containing
    - Aliskiren, a direct renin inhibitor (DRI)
    - Amlodipine, a dihydropyridine calcium channel blocker (DHP CCB)
- FDA-Approved Indications
  - Hypertension:
    - As initial therapy in patients likely to need multiple drugs
    - In patients not adequately controlled with monotherapy
    - As a substitute for the titrated components
- Conclusion
  - Tekamlo offers no clinical advantage in terms of efficacy or safety over current formulary alternatives
  - No positive clinical outcomes have been reported with the aliskiren component

Olmesartan/ Amlodipine/Hydrochlorothiazide Tablets (Tribenzor; Daiichi Sankyo)

Tribenzor

- Type of drug
  - Fixed-dose combination antihypertensive, containing
    - Olmesartan, an angiotensin receptor blocker (ARB)
    - Amlodipine, a dihydropyridine calcium channel blocker (DHP CCB)
    - Hydrochlorothiazide, a thiazide-type diuretic
- FDA-Approved Indications
  - Hypertension:
    - Substituted for its individually-titrated components
    - Used as add-on/switch therapy to provide additional blood pressure lowering for patients not adequately controlled on agents from 2 of the following classes: ARBs, CCBs, and diuretics at their maximally tolerated, labeled, or usual dose
  - NOT indicated for initial therapy
- Conclusion
  - Tribenzor offers no compelling clinical advantages in efficacy or safety over current formulary alternatives
  - It is unclear what resolution will come to the FDA's safety concerns about excess mortality in the ORIENT and ROADMAP (unpublished) studies

Donepezil 23mg
(Aricept 23mg; Eisai)

Donepezil 23 mg

- Type of Drug
  - Acetylcholinesterase inhibitor; enhances cholinergic function
  - Generic formulations of 5 and 10 mg tabs and ODT available Nov 2010

- Conclusion
  - Donepezil 23 mg is higher strength formulation of donepezil 5 and 10 mg tabs, which are now available in generic formulation
  - 23 mg formulation has different kinetics than giving 2 x 10 mg tablets
  - The one clinical trial used to gain FDA approval comparing 23 vs. 10 mg showed statistically significant improvement in measures of cognition but no benefit in improving global functioning
  - Efficacy of 23 mg is similar to giving 10 mg + memantine
  - Tolerability will be limited by increased incidence of AEs, particularly GI
  - Questionable if 23 mg offers clinically relevant improvement in symptoms vs. 10 mg, but AD has relentless progressive course, and FDA did allow approval

Ondansetron Oral Soluble Film (Zuplenz; Strativa)

Ondansetron Oral Soluble Film

- Type of Drug
  - 5-HT_3 antagonist; antinausea and antiemetic agent
  - Only oral soluble film of the newer antiemetics
  - Requires saliva
  - Packaged in foil packs/10 per box
- Conclusion
  - Ondansetron oral soluble film is expected to offer the same clinical benefits and outcomes as ondansetron ODT, but no relevant advantage
  - Approval based on efficacy and safety data from ondansetron ODT
  - Based on the available safety data, there are no clinically relevant differences between ondansetron oral soluble film and other ondansetron formulations

Glucocard 01 & Vital; Nova Max; Embrace

Self-Monitoring Blood Glucose Systems (SMBGS)
Test Strips & Meters

New Test Strips
UF Candidates

Manufacturer	BG System	FDA Approval	BG Testing Strip
Arkray USA	Glucocard 01	June 2008	Glucocard 01
	Glucocard 01 Mini	October 2008	Glucocard 01
	Glucocard Vital	October 2009	Glucocard Vital
Omnis Health	Embrace	May 2008	Embrace
Sanvita	Nova Max Plus	January 2010	Nova Max
	Nova Max Link	March 2008	Nova Max

Final UF candidate: 6 BG meters; 4 strips

Clinical Effectiveness Conclusion Test Strips

- All new test strips utilize auto coding or no coding technology
- Accuracy testing performed by the manufacturer shows that all new test strips meet the FDA and ISO standards
- With new test strips, a small sample size is required, test results are produced quickly, and alternate site testing can be used
- All products utilize glucose oxidase, not GDH-PQQ

GDH-PQQ: glucose dehydrogenase pyrroloquinoline quinone

Clinical Effectiveness Conclusion Test Strips

- Nova Max offers ketone testing on the Nova Max Plus Meter and wireless communication with the insulin pump on the Nova Max Link Meter
- Embrace Meter offers a talking feature that speaks results/commands
- Glucocard 01, Glucocard Vital, Nova Max, and Embrace test strips are similar to other test strips included on the UF in terms of meeting the minimum technical requirements

New Drugs in a previously reviewed class Final Decision

Drug	BCF	UF	NF	Comments- PA issues
RAAS	None		Olmesartan/amlodipine/ HCTZ (Tribenzor) Aliskiren/amlodipine (Tekamlo)	Tekamlo and Tribenzor: nonformulary & non-step preferred; PA criteria & MN criteria apply Step-therapy (automated PA); the following are step-preferred drugs: losartan ±HCTZ telmisartan ±HCTZ telmisartan/amlodipine valsartan ±HCTZ valsartan/amlodipine valsartan/amlodipine/HCTZ
Alzheimer's			Donepezil 23 mg (Aricept 23 mg)	
Antiemetic			Ondansetron soluble film (Zuplenz)	
BG Test Strips		Glucocard 01test strips Glucocard Vital test strips Embrace test strips	NovaMax strips	

Review of May 2011 P&T Activities

Dave Meade, PharmD, BCPS
Clinical Pharmacist

May 2011
DoD P&T Committee Meeting

- **Uniform Formulary Class Reviews**
  - Antipsychotic Agents
  - Nasal Allergy Drugs
- **New Drugs in Previously Reviewed Classes**
  - Bromfenac (Bromday ophthalmic soln)
  - Dutasteride/tamsulosin (Jalyn)
  - Saxagliptin /metformin extended-release (Kombiglyze XR)

May 2011
DoD P&T Committee Meeting

- **Utilization Management (Prior Authorization)**
  - Dabigatran (Pradaxa) Prior Authorization
  - Buprenorphine Transdermal System (Butrans) - Quantity Limits
  - Alsuma (Sumatriptan Inj) QL

May 2011
DoD P&T Committee Meeting

- For additional information regarding the May meeting, go to the website below: http://www.tricare.mil/pharmacy/BAP/
- This information remains as pre-decisional until Dr. Woodson signs the minutes for approval and implementation

Fluticasone (Flonase) update

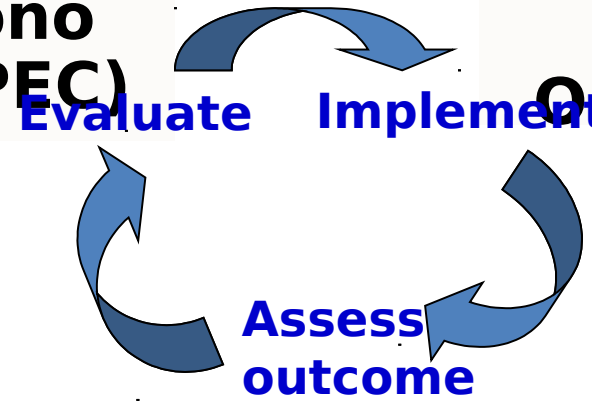
- One of the worst allergy seasons on record
- Lost multiple generic fluticasone manufacturers
  - SHORTAGE
- Recommended product
  - 00054-3270-99; Fluticasone 50mcg Nasal Spray 16gm, Roxane $7.54

Pharmacy Outcomes Research Team (PORT) Update

Shana Trice, PharmD
Clinical Pharmacist

The PORT and the PEC and the P&T
3 "P"s in a POD

Pharmacoeconomic Center (PEC)



Pharmacy Operations Center (POC)

Pharmacy Outcomes Research Team (PORT)

- Co-located
  - HQ in Falls Church, VA (TRICARE Pharmaceutical Operations Directorate (POD)
    - Director (PORT and Utilization Management), 1 analyst
  - PEC at Fort Sam Houston in San Antonio, TX
    - 1.5 pharmacists + interested clinical operation staff members
    - 2 pharmacoeconomists
- Mission: Improve patient outcomes and enhance the quality of the Military Health System pharmacy benefit through research and education

PORT Analyses/Activities

- Cost effectiveness reviews for P&T
- Formulary changes (“closing the loop”)
  - Effects of Tier 3 status (2 studies)
  - Effects of step therapy, clinical impact (PPI study)
- Past and potential policy changes
  - Fentanyl patch safety edit, polypharmacy pilot, Pharmacy & MTM (survey, future studies?)
- Patterns of use and prescribing/utilization patterns
  - TIBS, statins, antidiabetics, atypical antipsychotics

PORT Analyses/Activities

- Drug therapy and patient outcomes (ongoing research projects)
  - Chronic renal failure and NSAID use
  - Effects of LLT in secondary CHD population
  - ICS/LABA combos in asthma/COPD
  - Weekly vs. monthly bisphosphonates & adherence
  - Effects of copay on adherence (including $0 copay at MTFs)
- Pharmacy UM topics and questions
  - Comparative costs across POS
- Pharmacy data issues / information products
- Data access

Future Topics

- Step therapy as a formulary management tool
  - Especially statins, antidiabetics
- Atypical antipsychotics
  - Active Duty, >65, <18
- More integration of medical outcomes
- Upcoming drug classes
  - NSAIDs, depression/pain, ADHD/narcolepsy, anti-platelet, sleepers

Update on PEC Uniform Formulary webpage

Jeremy Briggs, PharmD
Industry Liaison

Update on Dabigatran (Pradaxa)

Angela Allerman, PharmD
Clinical Pharmacist

Dabigatran Background

Parameter	Comments
Type of Drug	• Direct thrombin inhibitor; approved 10/2010
UF Drug class / Previous UF Decision	• Anticoagulants • No previous UF decision; warfarin currently BCF
Strengths / Dosing	• 75 mg, 150 mg capsules • BID dosing (↓ dose in renal dysfxn)
FDA Indications	• ↓ risk of stroke in non-valvular Afib
Lab monitoring	• Not required for efficacy
Interactions	• Drug-Drug – fewer than with warfarin (amiodarone) • Drug-Diet – none
AEs	• Dyspepsia, GIB, ICH
Packaging	• Retain in original container
FSS Cost	• $4.90/day vs. $0.03 warfarin 5 mg

Dabigatran
Efficacy for Afib – RE–LY

- RCT, DB dabigatran vs. open label warfarin, non-inferiority
- N=18k pts with Afib + 1 other stroke risk factor; Age 71 yrs; 60% M
- Dabigatran (110 or 150 mg BID) vs. warfarin (INR 2-3)
- 1◦ Endpoint: ischemic or hemorrhagic stroke at 2 years
- INR within goal 64% of time (TTR); ASA use in 20% of pts

Outcome (/yr)	**Warfarin**	**Dabigatran 150 mg**	**P value**	**RR**
Stroke /systemic embolism	1.69%	1.11%	p<0.001	0.66 (0.53-0.82)
Stroke	1.2%	0.92%	p<.001	0.76 (0.6-0.99)
Hemorrhagic stroke	0.38%	0.1%	p<.001	0.26 (0.14-0.49)
Major bleed	3.6%	3.3%	P=0.31	0.93 (0.81-1.07)
GIB	1.02%	1.51%	p<0.001	1.50 (1.19-1.89)
MI	0.53%	0.74%	0.048	1.38 (1-1.91)

Randomized Evaluation of Long-Term Anticoagulation Therapy NEJM

Dabigatran
Efficacy for Off-Label Uses

- VTE prevention
  - Approved in Europe/Canada for VTE prevention following knee or hip replacement surgery, based on comparative trials with enoxaparin
  - 4 non-inferiority trials (RE-MODEL, RE-NOVATE, RE-NOVATE II, RE-MOBILIZE)
  - Dose 220 mg QD

- Acute VTE treatment
  - RE-COVER
  - Dabigatran vs. warfarin, R, DB, non-inferiority x 6 mos
  - 1◦ endpoint: recurrent, sx, objectively confirmed VTE & related death
  - Results:
    - Recurrent VTE/death: 2.4% dabigatran vs. 2.1% warfarin (difference 0.4, 95% CI -0.8 to 1.5; $p<0.001$)
    - Major bleed 1.6% dabigatran vs. 1.9% warfarin
    - Warfarin INR in goal 60% of time

Dabigatran Pipeline Drugs

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	Thrombin	Factor Xa	Factor Xa	Factor XA
FDA Status*	Approved	Investigational NDA: 11/2011*	Investigational Mid-2011*	Investigational Filing unknown
Brand Name	Pradaxa	Xarelto	Eliquis	
Mfg	B-Ingelheim	J&J	BMS/Pfizer	Daiichi-Sankyo
Dosing	BID	QD	BID	
Indications*	AFib Ortho prophylaxis VTE treatment	AFib Ortho prophylaxis VTE treatment VTE prophylaxis in medical pts ACS	AFib Ortho prophylaxis VTE treatment VTE prophylaxis in medical pts ACS	Afib VTE tx

*Proposed indications in *ital*

Dabigatran
DoD UF Review; Supportable/unsupportable uses

- DoD P&T Committee Uniform Formulary review
  - Mid-2012
  - Awaiting competition for dabigatran
- Supportable
  - Non-valvular Afib stroke prevention
  - VTE treatment
  - VTE prophylaxis hip/knee replacement
- Non-supportable
  - Valvular Afib stroke prevention
  - Tx of actue stroke
  - Acute Coronary Syndromes
  - VTE prevention in hypercoagulable conditions (Protein C, Protein S, antithrombin III deficiency)
  - Bridging for DCC

Upcoming Webcast: MTF Lock-in Edit and Impact of CHCS Drug Entries

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Clinical Pharmacist

MTF Lock-in Edit and Impact of CHCS Drug Entries: Webcast Information

TOPIC:

- MTF Prescription Restriction Program and a new MTF Lock-in PDTS Edit related to the restriction program
- The impact of creating CHCS drug entries for use with Sole Provider or other clinical programs on PDTS, and recommendations for how to minimize the cost and clinical impact of these CHCS drug entries

DATE: 23 June at 0800 and 1600 CST (same content will be presented twice)

DCO information:

AM (0800 CST/0900 EST) Session: https://connect.dco.dod.mil/r84664631

PM (1600 CST/1700 EST) Session: https://connect.dco.dod.mil/r32958460

Dial-in information: 1-877-939-1543 PC: 9750006

Questions?

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